Patent Claims

1. A method for the investigation of cytosine methylation in DNA sequences characterized in that

a) the DNA to be investigated is hybridized to at least one oligonucleotide of a defined methylation status,

b) the DNA-oligonucleotide hybrids of a) are reacted with at least one hemi-methylation sensitive restriction enzyme,

c) the occurrence or non-occurrence of a restriction is detected,

d) the methylation state of the investigated DNA is concluded.

2. The method according to claim 1, further characterized in that the oligonucleotides are bound to a solid phase.

3. The method according to at least one of the preceding claims, further characterized in that the oligonucleotides carry at least one detectable label.

4. The method according to at least one of the preceding claims, further characterized in that the oligonucleotides are labeled with a reporter dye and a quencher molecule.

5. The method according to at least one of the preceding claims, further characterized in that a plurality of oligonucleotides of identical sequence are used wherein said plurality consists of two parts wherein the first part of said oligonucleotides is methylated and the second part is unmethylated.

6. The method according to at least one of the preceding claims, further characterized in that the methylated and unmethylated oligonucleotides bear different labels.

7. The method according to at least one of the preceding claims, further characterized in that several oligonucleotides of different sequences are used.

8. The method according to at least one of the preceding claims, further characterized in that the oligonucleotides are immobilized on a sensitive surface.

9. The method according to claim 8, further characterized in that the modifiable properties of said surface are selected from the group consisting conductivity, characteristic frequency and surface tension.

10. The method according to at least one of claims 8 to 9, further characterized in that the surface comprises a piezoelectric crystal.

11. The method according to at least one of the preceding claims, further characterized in that a restriction enzyme is used which preferably cleaves unmethylated and hemi-methylated DNA as opposed to homogenously methylated DNA.

12. The method according to at least one of the preceding claims, further characterized in that the enzyme is selected from the group consisting AcsiI; AdeI; AscI; HinPI; ClaI; EciI; HinP1I; Hpy99I; NruI; RsrII; SalI.

13. The method according to at least one of claims 1 to 11, further characterized in that a restriction enzyme is used which preferably cleaves unmethylated DNA as opposed to hemi-methylated and homogenously methylated DNA.

14. The method according to at least one of the preceding claims, further characterized in that a plurality of different restriction enzymes are utilized simultaneously or sequentially.

15. Use of the method according to claims 1 to 14 for the diagnosis of cell

proliferative disorders (including cancer) or other diseases associated with a change in the cytosine methylation status, for predicting undesired drug effects, for distinguishing cell types, for distinguishing tissue types, and/or for investigating cell differentiation.

16. Use of hemi-methylation sensitive restriction enzymes for methylation analysis Associated with the diagnosis of cell proliferative disorders (including cancer) or other diseases associated with a change in the cytosine methylation status, for predicting undesired drug effects, for distinguishing cell types, for distinguishing tissue types, and/or for investigating cell differentiation.

17. Use according to claim 16, further characterized in that one of the following restriction enzymes is used: AcsiI; AdeI; AscI; HinPI; ClaI; EciI; HinP1I; Hpy99I; NruI; RsrII; SalI.

18. A test strip, comprising a plurality of immobilized oligonucleotides of a plurality of methylation statuses and/or sequences.

19. A kit comprised of at least one oligonucleotide, at least one hemi-methylation sensitive restriction enzyme and reaction buffers.